Remarks

Consideration of the previously submitted Information Disclosure statement and withdrawal of objections is greatly appreciated.

Amendments to the Claims

Claims 1, 3-5, and 7-11 are pending upon entry of this amendment. Claim 2 has been canceled. Claims 3 and 7 have been amended to depend from claim 1. Independent claim 1 has been amended to incorporate the limitations of canceled claim 2 and amended claim 6. Support for this amendment can be found in the specification, for example, on page 8, lines 3-8. Applicants believe that it is proper for the present amendment to be entered since it places the application in condition for allowance. Alternatively, entry of this amendment is proper since it places the claims in better form for appeal, does not raise any new issues, and does not require further consideration or search.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-11 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The best evidence against the examiner's rejection is the prior art article discussed below, cited as disclosing the claimed subject matter. O'Hagan, J. Pharm. Pharmacol. 50:1-10 (1997), **dated four years before the priority date of this application,** makes clear that even as of 1997,

nucleic acid vaccines, while not being perfect and having some FDA issues, were effective and could be delivered using a polymeric carrier.

Additional papers are enclosed with this response to show that DNA vaccines are considered to be enabled and vaccination with them does not require "undue experimentation". See Pachuk, et al. Curr Opin Mol Ther. 2(2):188-98 (April 2000); Barnes, et al. Curr Opin Mol Ther. 2000 Feb;2(1):87-93 (February 2000); and Watts and Kennedy Int. J. Parasitol. 29(8):1149-63 (1999) ("Watts").

The Legal Standard

The Court of Appeals for the Federal Circuit (CAFC) has described the legal standard for enablement under § 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art, without undue experimentation (*See e.g. Amgen v. Hoechst Marion Roussell* 314 F.3d 1313 (Fed. Cir. 2003); *Genentech, Inc. v. Novo Nordisk A/S*, 108 F3d at 165, 42 USPQ2d at 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (*M.I.T. v. A.B. Fortia*, 774 F.2d 1104 (Fed. Cir. 1985)).

Whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See *In re Wands*, 858 F.2d 731, 735, 736-737, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir.1988). As set forth in *Wands*, the factors to be considered in determining whether a

claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." *Atlas Powder Co., v. E.I. DuPont De Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir.1984). There is no requirement for examples.

Claims 1, 3-5, and 7-11 are enabled

The specification discloses to one of ordinary skill in the art how to make and use the claimed composition without undue experimentation. With respect to the examiner's comments, the claims are not drawn to "gene therapy art," page 5 of the office action, line 20. The amended claims define a vaccine composition for inducing an immune response to a pathogen that contains a nucleic acid encoding an antigen eliciting an immune response to the pathogen encapsulated in a mucoadhesive controlled release particulate formulation. The composition can be formed by a method that contains the following steps: (1) lyophilizing a solution of a biodegradable polymer to form an open-celled polymeric foam of approximately 95% void volume, (2) impregnating the foam with an aqueous solution of the nucleic acid, (3) lyophilizing the foam to remove the water, and (4) extruding the resulting matrix at ultrahigh pressures.

Applying the *Wands* factors, it is clear from the amount of direction and guidance in the specification that sufficient detail is provided to one of ordinary skill in the art to make and use the claimed composition.

The quantity of experimentation, the state of the prior art, the relative skill of those in the art, and the predictability of the art

A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). The genetic manipulation of plasmid DNA is **highly** routine in the art. As described in the enclosed article by Watts, Watts and Kennedy Int. J. Parasitol. 29(8):1149-63 (1999) ("Watts"), plasmid vectors can be rapidly constructed and easily tested. All that is required is the antigen DNA sequence. Watts and the specification on pages 4-6 and pages 11-17, for example, disclose a number of DNA vaccines for bacterial, viral, and parasitic pathogens. Therefore, the creation of numerous, different plasmids encoding antigens from a variety of pathogens would be routine experimentation for one of ordinary skill in the art, because the relative skill of those in the art is high.

The amount of direction and guidance presented, the presence of working examples, the nature of the invention

The specification discloses the encapsulation of DNA into a biodegradable polymer to achieve slow release into the system, pages 17-20. The specification discloses the addition of a mucoadhesive, pages 21-23. The specification discloses the formation of the vaccine composition by a method including the steps of lyophilizing a solution of a biodegradable polymer to form an open-celled polymeric foam of approximately 95% void volume, impregnating the foam with an aqueous solution of the nucleic acid, lyophilizing the foam to remove the water, and extruding the resulting matrix at ultrahigh pressures, pages 27-28. The specification discloses administration of the vaccine, page 32. The specification provides *in vitro* data verifying antigen release, pages 29-31. Finally, the specification provides *in vivo* data in BALB/c mice immunized with vaccine/PLGA particles, PLGA-alone, or a control oligodeoxynucleotide/PLGA particles verifying protective immunity only in mice immunized with the pDNA/PLGA vaccines, pages 32-33. As noted above, there is **no** requirement for examples. The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

The breadth of the claims

The specification discloses the claimed composition in such detail that one skilled in the art would be able to make and/or use the invention without undue experimentation. Thus the claims, as amended, are enabled by the specification.

Rejection Under 35 U.S.C. § 102

Claims 1-5 and 8-11 were rejected under 35 U.S.C. § 102(b) as being anticipated by O'Hagan, J. Pharmacy and Pharmacology 50(1): 1-10 (1998) ("O'Hagan"). Applicants respectfully traverse this rejection.

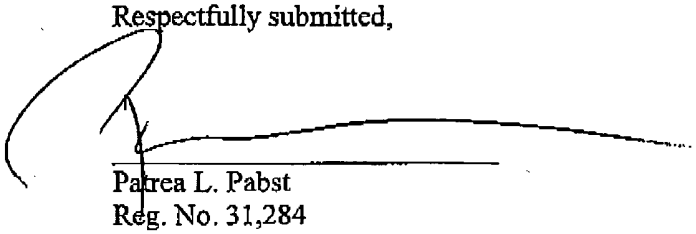
O'Hagan describes vaccines, including vaccines made by recombinant DNA technology and nucleic acid based vaccines. O'Hagan discloses the use of biodegradable polymers as vaccine adjuvants, in particular, the encapsulation of **protein** antigens into poly(lactide-co-glycolides) microparticles and the use of emulsions formed of materials such as mineral oil, and those which are advantageous for mucosal administration.

O'Hagan does not disclose encapsulating nucleic acid vaccines in a polymeric foam material. While O'Hagan states that delivery of a vaccine composition by mucosal administration would be "ideal" (Table 1, p. 2), the reference does not teach or suggest enhancing antigenicity by increasing **mucoadhesion**.

Therefore O'Hagan neither discloses nor makes obvious the claimed subject matter.

Allowance of claims 1 and 3-11 as amended is respectfully solicited.

Respectfully submitted,



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